REMARKS/ARGUMENTS

Reconsideration and withdrawal of the rejections in the outstanding Office Action are respectfully requested in view of the foregoing amendments and the following remarks.

Interview Summary

Applicants thank the Examiner for granting a telephone interview with Applicants' representatives Arnold Turk and Chuck Niebylski on November 30, 2005. During the interview, proposed amendments and arguments were presented and discussed with the Examiner, with the Examiner indicating that the amendments discussed during the interview would require further search and consideration. Accordingly, the Examiner indicated that the amendments and arguments be submitted in writing in a Request for Continued Examination, and indicated the same in the interview summary dated December 2, 2005.

During the interview, the amendments presented herein were discussed with the Examiner, and arguments in support of the amendment and distinguishing the claims over the prior art utilized in the rejections of record. The amendments and arguments are set forth in the amendments and arguments herein.

Summary of Status of Amendments and Office Action

In the present amendment, claims 1 and 17 are amended. Claims 1 and 3-19 are pending in the application, with claims 1 and 6 being independent.

Applicants have amended the specification in accordance with MPEP §310 by adding a paragraph at page 1, line 1, to make reference to the rights of the U.S. government in the invention arising from the awarding of Grant No. RO1 CA68011 by The National Institutes of Health, National Cancer Institute. The grant was awarded to co-inventor Dr. Leong as principal investigator. Applicants also cancel the paragraph at page 6, lines 1-3, as being redundant in view of the new paragraph added above at page 1, line 1.

Applicants have amended the claims to more clearly recite the claimed subject matter. Claim 1 has been amended to recite, in-part, "a microparticle comprising a fragment of solidified tumor tissues or cells, without soluble tumor antigen from the solidified tumor tissues or cells being present in a soluble form". Support for this amendment is found in the application as filed. For example, support for the amendment is found in the paragraph bridging pages 7 and 8 describing embodiments where the soluble antigen is bound to a variety of insoluble components. Also, for example, page 19, lines 1-24, describes preparing tumor fragments including precipitation of the fragments followed by washing to remove the supernatant that would contain soluble components. Further, page 21, lines 16-30, describes how the supernatant fraction contains soluble antigen and that such soluble antigen may then be bound to microspheres, rendering the antigen insoluble, and then used in a vaccine. These disclosures indicate that at the time of invention, the inventors were in possession of making and using a microparticle comprising a fragment of solidified tumor tissues or cells, without soluble tumor antigen from the solidified tumor tissues or cells being present in a soluble form.

Claim 17 has been amended to reflect the amendment of claim 1, and recite wherein the fragment comprises ground tumor tissues or cells wherein soluble tumor antigen has been removed. Support for this amendment is found in the specification, for example, as discussed above, at the paragraph bridging pages 7 and 8, at page 19, lines 1-24, and at page 21, lines 16-30. No new matter is added.

Information Disclosure Statements

The Office Action indicates that the Information Disclosure Statement filed February 29, 2004, "has been considered to the extent that the Examiner could understand". Applicants note that Chinese Application No. 1119459 was crossed out for a lack of an English translation, even though the Office Action indicates that the English abstract of the document was considered as was the English translation of the related Office Action.

Applicants submit that concise English-language explanations of the relevance of the cited documents were included in the Third Supplemental Information Disclosure Statement filed February 29, 2004 in accordance with Patent and Trademark Office practice. This included an English translation of the Chinese Office Action and an English abstract of Chinese Application No. 1119459. MPEP §609.04(a) states (emphasis added):

> Each information disclosure statement must further include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information listed that is not in the English language. Submission of an English language abstract of a reference may fulfill the requirement for a concise explanation. Where the information listed is not in the English language, but was cited in a search report or other action by a foreign patent office in a counterpart foreign application, the requirement for a

> concise explanation of relevance can be satisfied by submitting an English-language version of the search report or action which indicates the degree of relevance found by the foreign office. This may be an explanation of which portion of the reference is particularly relevant, to which claims it applies, or merely an "X", "Y", or "A" indication on a search report.

Furthermore, if the Applicants meet these requirements for a non-English language document then the Examiner must indicate that it has been considered in the same manner as consideration is indicated for information submitted in English. This is clearly stated in MPEP 609.05(b) (emphasis added):

> Information which complies with requirements as discussed in this section but which is in a non-English language will be considered in view of the concise explanation submitted (**>see MPEP § 609.04(a), subsection III.<) and insofar as it is understood on its face, e.g., drawings, chemical formulas, in the same manner that non-English language information in Office search files is considered by examiners in conducting searches. The examiner need not have the information translated unless it appears to be necessary to do so. The examiner will indicate that the non-English language information has been considered in the same manner as consideration is indicated for information submitted in English. The examiner should not require that a translation be filed by applicant. The examiner should not make any comment such as that the non-English language information has only been considered to the extent understood, since this fact is inherent. See *Semiconductor Energy Laboratory Co. V. Samsung Electronics Co.*, 204 F.3d 1368, 1377-78, 54 USPQ2d 1001, 1008 (Fed. Cir. 2000) ("[A]s MPEP Section 609C(2) reveals, the examiner's understanding of a foreign reference is generally limited to that which he or she can glean from the applicant's concise statement. Consequently, while the examiner's initials require that we presume that he or she considered the [foreign] reference, this presumption extends only to the examiner's consideration of the brief translated portion and the concise statement.").

Applicants submitted copies of Chinese Application No. 1119459, an English language abstract thereof, a Chinese Office Action related to Chinese Application No. 1119459, and an English Translation of the Chinese Office Action. Therefore, in

accordance with Patent and Trademark Office procedure set forth at MPEP §609.04(b), the Examiner should indicate consideration of Chinese Application No. 1119459 in the same manner as consideration is indicated for information submitted in English. Accordingly, Applicants are submitting a Form PTO-1449 listing this document. The Examiner is respectfully requested to forward an initialed copy of the form with the next communication from the Patent and Trademark Office.

Rejection Under 35 U.S.C. 102(b)

Hiserodt

Claims 1, 3, 6, and 7 remain rejected under 35 U.S.C. 102(b) as being anticipated by WO 98/16238 to Hiserodt et al. ("Hiserodt"). Claim 2 is canceled. Claims 4-5 and 8-19 were not included in the rejection. The rejection asserts that Hiserodt at page 23, lines 5-9, discloses a vaccine comprising the tumor tissue particle in combination with "isolated or recombinant cytokines".

In regard to "a source of tumor antigen", the rejection asserts that "an alternative source of tumor-associated antigen" includes "tumor cell homogenate, detergent lysate, or a purified derivative thereof", (see page 6, lines 38-40), and that "[c]ancer cells for use as tumor antigen source can be...fixed" (see page 15, lines 20-25). The rejection asserts that Hiserodt discloses a tumor vaccine comprising tumor tissue homogenate, and isolated or recombinant cytokine. Applicants traverse the rejection for the reasons of record, and for the additional reasons below.

Hiserodt Fails to Teach All Recited Claim Limitations

However, solely to more clearly describe the subject matter of the invention, and without acquiescence, agreement, or acceptance of the rejection, the Applicants have amended claim 1 to recite a microparticle comprising a fragment of solidified tumor tissues or cells, "without soluble tumor antigen from the solidified tumor tissues or cells being present in a soluble form". Similarly, claim 17 has been amended to clarify that the fragment comprises ground tumor tissues or cells "wherein soluble tumor antigen has been removed." Support for these amendments are found in the specification, and examples of such support are described above.

Applicants submit that Hiserodt's tumor tissue or cell homogenate comprises soluble tumor antigen. Accordingly, Applicants submit that the instant claims are distinguished from Hiserodt because Hiserodt does not teach or suggest a tumor vaccine comprising a microparticle comprising a fragment of solidified tumor tissues or cells, without soluble components from the solidified tumor tissues or cells being present in a soluble form. For at least this reason, Applicants respectfully request reconsideration and withdrawal of the rejection.

Hiserodt Does Not Inherently Anticipate All Recited Claim Limitations

Additionally, Applicants point out that claim 1 recites, in part, a microparticle comprising a fragment of solidified tumor tissues or cells, and "said fragment being of a size so as to allow phagocytosis of the fragment". The final rejection appears to assert that Hiserodt's homogenates inherently comprise the recited claim feature of the "fragment being of a size so as to allow phagocytosis of the fragment". In order to prove

anticipation by inherency, the U.S. Patent and Trademark Office must show evidence which "must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." Emphasis added, Continental Can Co. USA v. Monsanto Co., 948 F.2d 1264, 1268 (Fed. Cir. 1991).

The Examiner is reminded that in order for inherency to be present the Examiner has the burden of showing that the result indicated by the Examiner is the necessary result, and not merely a possible result. In re Oelrich, 212 U.S.P.Q. 323 (CCPA 1981); Ex parte Keith et al., 154 U.S.P.Q. 320 (POBA 1966). The fact that a prior art article may inherently have the characteristics of the claimed product is not sufficient. Ex parte Skinner, 2 U.S.P.Q.2d 1788 (BPAI 1986).

As the Board of Patent Appeals and Interferences states in Ex parte Levy, 17 U.S.P.Q.2d 1461, 1463:

> However, the initial burden of establishing a prima facie basis to deny patentability to a claimed invention rests upon the examiner. In re Piasecki, 745 F.2d 1468, 223 USPQ 785 (Fed. Cir. 1984). In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art. In re King, 801 F.2d 1324, 231 USPQ 136 (Fed. Cir. 1986); W.L. Gore & Associates, Inc. v. Garlock, Inc., 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983); In re Oelrich, 666 F.2d 578, 212 USPQ 323 (CCPA 1981); In re Wilding, 535 F.2d 631, 190 USPQ 59 (CCPA 1976); Hansgirg v. Kemmer, 102 F.2d 212, 40 USPQ 665 (CCPA 1939).

Applicants submit that the rejection does not meet the required burden. Hiserodt teaches at page 6, lines 38-40, that "the inactivated tumor cell may be substituted by an alternative source of tumor associated antigen, such as tumor cell homogenate, detergent lysate, or a purified derivative thereof, such as an isolated protein". The

rejection does not provide any support that Hiserodt's homogenates necessarily contain fragments of tumor tissues or cells of a size that would allow phagocytosis.

In view of the above, Applicants respectfully subject that the rejection of claims 1-3, 6, and 7 under 35 U.S.C. 102(b) should be withdrawn.

Rejection Under 35 U.S.C. 103(a)

Hiserodt in view of Pardoll

Claims 1, 4, 5, and 8-19 are rejected under 35 U.S.C. 103(a) as being obvious over Hiserodt in view of U.S. Patent No. 5,861,159 to Pardoll et al. ("Pardoll").

The rejection applies Hiserodt as discussed above as allegedly disclosing a tumor vaccine comprising tumor tissue homogenate, and isolated or recombinant cytokine. The rejection admits that Hiserodt does not teach controlled release vehicle containing GM-CSF. The rejection, however, asserts that Pardoll teaches a pharmaceutical composition comprising controlled release vehicle containing GM-CSF and a tumor antigen. The rejection then concludes that it would have been obvious for one of ordinary skill in the art to make and use Pardoll's controlled release vehicle containing GM-CS in the place of Hiserodt's at least one isolated cytokine with Hiserodt's tumor tissue cell homogenate with a reasonable expectation of success for cancer immunotherapy. Applicants respectfully traverse the rejection as follows.

Claim 1 recites a microparticle comprising a fragment of solidified tumor tissues or cells, "without soluble components from the solidified tumor tissues or cells being present in a soluble form". As argued above, Applicants submit that Hiserodt's tumor tissue or cell homogenate comprises soluble tumor antigen. Applicants submit that

Hiserodt neither teaches or suggests a tumor vaccine that uses a microparticle comprising a fragment of solidified tumor tissues or cells, without soluble components from the solidified tumor tissues or cells being present in a soluble form.

Further, whether or not one having ordinary skill in the art would have motivation to combine the disclosures of Hiserodt and Pardoll, Hiserodt taken together with Pardoll, also fails to teach or suggest a tumor vaccine that uses a microparticle comprising a fragment of solidified tumor tissues or cells, without soluble components from the solidified tumor tissues or cells being present in a soluble form. Therefore, Applicants submit that the instant claims are not obvious over the combination of recited documents because the combination does not teach or suggest all of the recited features of the instant claims.

Accordingly, Applicants respectfully request that the Office withdraw the rejection of claims 1, 4, 5, and 8-19 under 35 U.S.C. 103(a).

CONCLUSION

For the foregoing reasons, it is believed that all of the claims in this application are in condition for allowance, which action is respectfully requested.

If the Examiner has any questions, or wishes to discuss this matter, the Examiner is respectfully invited to contact the undersigned at the below-listed telephone number.

Respectfully Submitted,
Tadao OHNO et al.

Bruce H. Bernstein
Reg. No. 29,027

Arnold Turk
Reg. No. 33094

January 24, 2006
GREENBLUM & BERNSTEIN, P.L.C.
1950 Roland Clarke Place
Reston, VA 20191
(703) 716-1191